SPECIALTY DRUGS
A RICH PIPELINE THAT NEEDS TO BE MANAGED

Health plans will experience increasing demands as specialty drugs are used for more common conditions. The author discusses ways to manage the ever-changing terrain.

BY KEITH BRADBURY

The process of managing specialty drugs can sometimes be as complex as the conditions these medications are designed to treat. For example, the U.S. Food and Drug Administration has never set a formal definition for specialty drugs. PBMs and specialty pharmacies themselves often have slightly different drugs on their respective specialty drug lists. One thing that can be agreed upon is that clinicians, patients, and payers will see a lot more specialty drugs in the future, creating a greater need to ensure that these agents are used safely, effectively, and efficiently.

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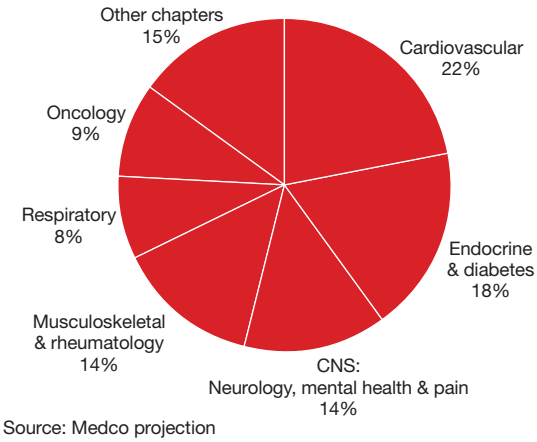
Some typical characteristics of specialty drugs:

- They are expensive, with annual costs ranging from $6,000 to more than $400,000
- Special handling, such as protection from light or refrigeration, may be necessary
- Recipients need comprehensive education, training, and compliance programs to support proper use
- The conditions being treated are complex and often chronic

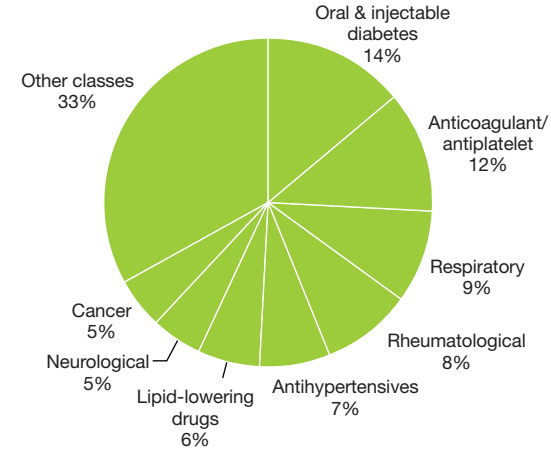
These medications are quickly becoming an important part of the healthcare landscape, accounting for 12.8 percent of all pharmacy spending during 2008 — an increase from 11.4 percent in 2007, according to Medco's *2009 Drug Trend Report*. Thus, specialty pharmacy drugs, as a category of medications, has become the largest single area of drug spending for plans, surpassing cholesterol-lowering medications by a significant margin. The growth rate for these drugs rose to 15.8 percent in 2008, after several years of brisk spending on specialty drugs. Based on the current trend for both specialty drugs and nonspe-

Top therapeutic chapters contributing to projected drug trend (2009–2011)



Source: Medco projection

Top therapeutic classes contributing to projected drug trend (2009–2011)



cialty drugs, by 2015, the former could account for 22 percent of all drug costs. The economics are reflected in the costs of many of these medications. An annual regimen of injectable multiple sclerosis drugs can cost greater than $20,000 annually, but more rare disorders, such as severe combined immunodeficiency disease, can require treatment that costs in excess of $250,000 per year.

The growth in this category should not be a surprise. Specialty drugs increasingly are being used for more common conditions, such as cancer, MS, and rheumatoid arthritis, as well as for assorted rare diseases, such as pulmonary arterial hypertension and hemophilia. Medco has found that about one third of new molecular entity approvals in recent years have been in the area of specialty drugs. In addition, the population of specialty drug users is expected to expand with new specialty treatments under development for lupus, Alzheimer's disease, retinal and other eye diseases, hereditary angioedema and asthma, gout, osteoarthritis, and osteoporosis. These high costs, combined with the growing demand for specialty drugs, is forcing health plans to ensure that every dollar spent is being used effectively for the right patients and that these patients are getting the greatest achievable benefit with these therapies.

KEY CATEGORIES

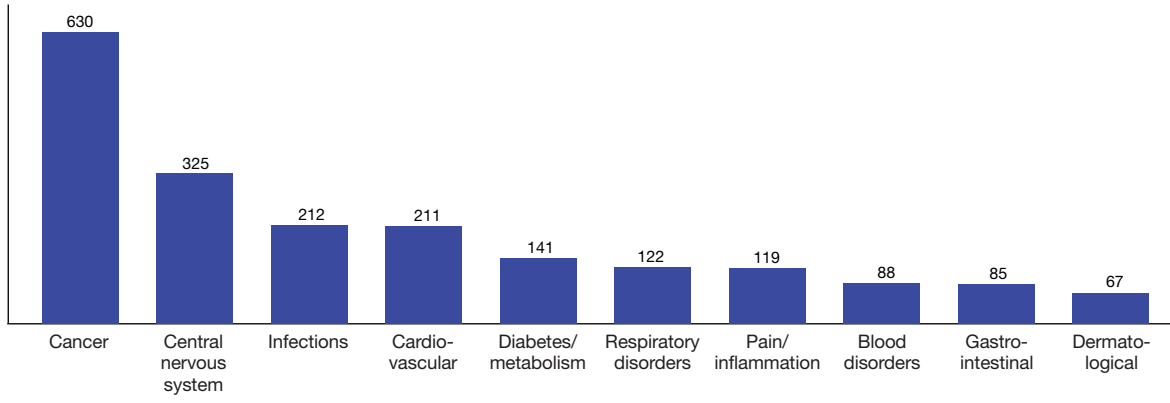
According to IMS Health forecasts, cancer agents could soon be the top category for specialty drugs, reaching $80 billion by 2012, driven both by the volume of patients and higher cost treatments. Medco is projecting total annual spending increases on cancer drugs between 12 and 14 percent during 2009, with a boost from the estimated 1.5 million newly diagnosed patients this year, and a similar growth rate for 2010. It also projects another increase of 11 to 13 percent in 2011. According to Pharmaceutical Research and Manufacturers of America, expanded indications for existing treatments and a deep pipeline exceeding 800 drugs will fuel growth in the years to come.

Early detection and better-tolerated medications allow cancer to be managed more like a chronic disease. The 5-year relative survival rate for all cancers between 1996 and 2004 was 66 percent, an increase from the 50 percent rates seen between 1975 and 1977 (ACS 2009). Longer courses of such medications as rituximab, erlotinib, lenalidomide, and pemetrexed are being used in place of short courses of cytotoxic chemotherapy. Imatinib, sunitinib, sorafenib, lapatinib, and nilotinib are targeted oral oncology drugs that have added greater convenience and tolerability to treatment, but some of these drugs can cost almost $10,000 a month.

RELIEVING PAIN

Although cancer drugs are an increasing part of the specialty category, similar developments are taking place in pain management. Millions of Americans live with chronic pain, including 27 million people with osteoarthritis (Arthritis Foundation 2008a), and millions of others suffer from chronic lower back pain and neuropathic pain that has resulted from damage or dysfunction of pain-transmitting nerve fibers. Pain has been traditionally treated with nonsteroidal anti-inflammatory drugs, opioid analgesics, and other analgesics, but these practices may soon change with the entry of tanezumab onto the market. Currently in phase 3 studies for osteoarthritis and chronic

Drugs in development by therapeutic area (2008)



Source: "From Pipeline to Market," R&D Directions, Vol. 14-6:6–7

lower back pain and phase 2 studies for the treatment of chronic pain, tanezumab inhibits the actions of nerve growth factor, opening a potentially huge market for specialty drugs. One study has shown that an injection once every 8 weeks reduces pain in patients with knee osteoarthritis who did not respond adequately to earlier treatments and were candidates for joint replacement (ACR 2008).

CROWDED RA MARKET

Specialty drugs have been a staple for nearly a decade in the treatment of RA, an autoimmune disorder affecting joints in 1.3 million patients (Arthritis Foundation 2008b), as well as in other autoimmune disorders, such as Crohn's disease, ankylosing spondylitis, and plaque psoriasis. Treatments for these conditions have led to great demand for specialty drugs. The American College of Rheumatology recommends the use of tumor necrosis factor inhibitors, a category of biologic response modifiers, in newly diagnosed RA patients with high disease activity, or RA patients who are not responding to methotrexate (Saag 2008). TNF inhibitors include etanercept, adalimumab, infliximab, certolizumab, and golimumab. Other biologics also have gained approval for RA treatment, including rituximab and abatacept. Last year, the FDA delayed the approval of tocilizumab, a treatment that targets interleukin 6, but approval is expected late this year or next year.

ORALS MAY RESHAPE MS

Beta-interferons are part of the specialty treatment for MS, a segment with 23.6 percent spending growth in 2008. The marketplace for these drugs gained a new entry in August with Novartis' version of interferon-beta 1b (Extavia), another branded version of Bayer's Betaseron. This new drug joins a marketplace that already counts glatiramer acetate and interferon-beta 1a (Rebif and Avonex) as first-line treatments. Natalizumab, which carries a risk of a very rare brain infection, is indicated for use when other treatments have failed.

In addition, several new oral treatments for MS are in the pipeline and could represent a dramatic change in treatment, which is now largely dominated by injectables. Fingolimod and an oral formulation of cladribine could drive higher costs in this category. One potential problem with these new oral treatments, however, may be the risk of severe immunosuppression. Existing injectable drugs have a good safety history that could slow the adoption of the newer oral medications. However, some oral drugs in the pipeline could be used in addition to current therapies.

OSTEOPOROSIS AND BONY METASTASIS

Oral bisphosphonates, such as generic alendronate, account for 75 percent of osteoporosis drug use, but specialty drugs, such as teriparatide, are increasingly used for patients who have a very high risk of fractures. New specialty treatments for osteoporosis are meant to counteract the effects of hormonal therapy, including those associated with cancer therapies. Amgen's denosumab, which has been shown to increase bone mass density in patients with breast and prostate cancers who take anti-estrogen or testosterone ablation therapies, had received a recommendation from an FDA panel for approval to treat osteoporosis in noncancer patients. However, on Oct. 19, the FDA asked for a formal plan for communicating denosumab's safety issues to doctors and women with osteoporosis, which is expected to delay introduction of the drug by several months. Regulators also asked for updated safety data.

FOCUS ON LUPUS

Approximately 1.5 million patients have lupus erythematous, a condition with no cure with treatments aimed at addressing symptoms (Lupus Foundation 2009). However, the market is close to having the first new treatments in 50 years. Several drugs have had difficulty showing efficacy in clinical trials, and other drugs are used off-label to prevent flare ups. However, progress recently has been made with drugs that address different targets. Ocrelizumab, which recruits the body's immune system to attack and destroy B-cells, is in a phase 3 trial to treat lupus nephritis, a form of lupus that attacks the kidneys. Human Genome Sciences (2009) recently reported positive phase 3 trial data for belimumab, which inhibits activity of the protein B-lymphocyte stimulator, as a treatment for systemic lupus erythematous. Epratuzumab targets the CD-22 antigen on b-lymphocytes and is presently in phase 2 clinical trials.

HEREDITARY ANGIOEDEMA

Hereditary angioedema can be a life-threatening genetic disorder caused by improper function of a serum protein called a C1 inhibitor. Deficiency or dysfunction of this protein leads to rapid swelling of the hands, feet, limbs, face, digestive tract, and windpipe. Antihistamines and other related treatments offer limited benefit in hereditary angioedema, which calls for intravenous (IV) fluids and pain reliev-

ers during a flare-up. Attenuated androgens, such as danazol, which are derivatives of normal sex hormones, can significantly reduce the frequency and severity of attacks. A number of C-1 esterase inhibitors are in development for this disorder. The first to gain FDA marketing approval is Viropharma's Cinryze, which is aimed at preventing flare-ups. Icatibant, a drug that inhibits bradykinin, was approved for treating hereditary angioedema in Europe, and is undergoing additional study. Ecallantide is yet another drug being studied for this disorder that works via a different mechanism from the drugs listed above.

About one third of new drug approvals in recent years have been in the area of specialty drugs, notes Keith Bradbury from Medco.

MANAGING SPECIALTY DRUGS

Health plan sponsors need to develop tools and programs to manage new specialty pharmacy drugs and their costs. One initial approach is to ensure the drugs are being supplied from the most efficient channel, and to cover them to the highest extent possible under the pharmacy rather than the medical benefit. Specialty pharmacy distribution provides greater transparency to benefit plans than if the drugs are covered through the medical benefit; the drug cost and dosage are spelled out clearly, rather than grouped within the bill of an office visit.

Specialty pharmacies also can:

- Develop preferred vendor relationships with manufacturers; this can generate savings in categories that are increasingly competitive, such as TNF inhibitors or MS treatments
- Have better access and contract for better prices for these medications than individual doctors
- Help to manage the clinical aspect of assisting patients in improving health outcomes, encouraging compliance with the therapy, and helping possibly avoid adverse events that can lead to treatment failure or other costs

Nurses and pharmacists at specialty pharmacies have the expertise to help patients properly administer their medications, especially when some require special equipment. For example, pulmonary hypertension treatments, such as epoprostenol or treprostinil, require continuous infusion; iloprost is administered multiple times per day via a special nebulizer. Several specialty drugs require risk evaluation and mitigation strategy (REMS) programs, which can include patient registries, limited distribution, enhanced patient monitoring, and other measures intended to reduce adverse drug events and improve safe administration.

Many patients using specialty pharmacy services are taking more than one drug, heightening the need for monitoring and counseling about potential drug interactions or other drug therapy-related issues. Drug utilization reviews can show whether patients are taking conflicting drugs. This can lead to safety improvements, more effective treatment, and less waste.

COVERAGE MANAGEMENT

Prior authorization or precertification help benefit plans to manage coverage of such specialty drugs as oncology agents, which are often used off-label but with some evidence of efficacy. When these high-cost drugs are used off-label without sufficient scientific evidence, however, they may not provide clinical benefits. The available clinical evidence can be used to support decisions about the benefit for patients, coverage of the therapy, and the duration of therapy that should be approved before another review is needed. Limits on the covered quantities of medication per month or other appropriate period can help align cost share amounts, minimize waste, and support dosing that is within clinical guidelines.

In addition to PAs and quantity limits, another approach is step therapy. In therapy classes with like competitors, lower cost specialty or nonspecialty drugs could be tried before more costly specialty drugs. This can be a useful approach where certain drug categories have a larger number of good options. These categories may include medications used to treat RA, psoriasis, inflammatory bowel disease, MS, and pulmonary arterial hypertension.

PREVENTING WASTE

After determining what channel will provide access to specialty medications and under which circumstances to cover them, programs need to be in place to help limit waste. Drugs should be dispensed in quantities that make clinical sense, not only for the sake of efficiency and cost savings, but also for the sake of safety.

For example, clinicians need to monitor the hemoglobin levels of patients using erythropoietin-stimulating agents and adjust or temporarily discontinue dosing accordingly. In the case of hepatitis C

treatments, there is no evidence that specialty drugs offer a clinical benefit when they are taken longer than 6 months to a year, depending on the viral genotype (Davis 2002). In some circumstances, therapy can be discontinued after 12 weeks if there is no response. Hemophilia patients, for example, could get clotting factor in concentrations that lead to more precise dosing and less waste.

Scientific innovation also can diminish waste. Pharmacogenomics — the use of gene or biomarker testing to help use drugs more effectively and safely — also can help providers determine which drugs are most appropriate. More and more, drug labels are incorporating this information, and there is an increasing amount of published medical literature that deals with this issue.

TIERING OPTIONS

Plan design can help lead to better cost management for employers and health plan sponsors. One option is to create a specialty drug tier that is based on a percentage of a drug's price with caps on the patient's out-of-pocket expense. However, a patient's ability to pay for these drugs needs to be taken into account when designing this tier. If a patient cannot pay for a medication, he or she is likely to be noncompliant with treatment and incur greater health risks. At the same time, as specialty drugs represent an increasingly greater part of plan drug spending, evaluating, and implementing this approach likely becomes even more critical. If drugs become too expensive or patients hit lifetime limits, pharmaceutical manufacturers have copayment assistance programs, and specialty pharmacies have reimbursement specialists who can assist patients in finding programs to help them pay for their medications.

BIOSIMILARS CUT COSTS

Presently, there is no avenue for "generic," or follow-on versions of biologic drugs to be brought to market, even though patents have expired on several billion dollars' worth of these medications. Follow-on versions of these drugs are expected to offer savings of up to 30 percent compared with brand name biologics (FTC 2009). There is still debate in Washington about the length of exclusivity that brand name treatments should have before facing follow-on biologic entrants. Biologics with approximately $32 billion of biologic drug sales today may have to go off patent by the end of 2015. The first wave of follow-on biologics could include human growth hormones, human insulins, filgrastim, and several other drugs.

THE PROMISE AND CHALLENGES OF SPECIALTY DRUGS

Specialty drugs will place increasing demands on health plans, but specialty pharmacy distribution can help manage the clinical and economic aspects of treating patients. These drugs will treat a broader range of conditions, while existing drugs will gain new indications, further expanding the marketplace. As this propels demand, health plans can assert greater control over their spending with the help of specialty pharmacies that provide greater transparency about the cost of treatment and increased patient support. Improved clinical management of these complex medical conditions can help lower the incidence of hospitalizations, emergency room visits, and other adverse events, which can help offset total healthcare costs that factor in hospital bills, disability claims, and rehabilitation costs. Patients also can gain greater convenience, and plans may realize cost savings when specialty infusion drugs can be provided to patients in their homes with appropriate nursing and other clinical support.

REFERENCES

ACR (American College of Rheumatology). New therapy may fight knee osteoarthritis pain. 2008. http://www.rheumatology.org/press/2008/2008_press_18.asp. Accessed Oct. 6, 2009.

ACS (American Cancer Society). Cancer Facts & Figures, 2009. «http://www.cancer.org/downloads/STT/500809web.pdf.» Accessed Oct. 6, 2009.

Arthritis Foundation. Osteoarthritis Fact Sheet. 2008a. «http://www.arthritis.org/media/newsroom/media-kits/Osteoarthritis_fact_sheet.pdf.» Accessed Oct. 6, 2009.

Arthritis Foundation. Rheumatoid Arthritis Fact Sheet. 2008b. «http://www.arthritis.org/media/newsroom/media-kits/Rheumatoid_Arthritis_Fact_Sheet.pdf. »Accessed Oct. 6, 2009.

Davis GL. Monitoring of viral levels during therapy of hepatitis C. *Hepatology*. 2002;36:S145–S151.

FTC (Federal Trade Commission). Emerging health care issues. Follow-on biologic drug competition. 2009. «www.ftc.gov/os/2009/06/P083901biologicsreport.pdf.» Accessed Oct. 6, 2009.

(Human Genome Sciences data. No authors listed.) Trial watch: BLYS-targeted antibody shows promise in phase III SLE trial. *Nat Rev Drug Discov.* 2009;8:688.

Lupus Foundation of America. About Lupus. 2009. «http://www.lupus.org/webmodules/webarticlesnet/templates/new_learnunderstanding.aspx?articleid=2232&zoneid=523.» Accessed Oct. 6, 2009.

Saag KG, Teng GG, Patkar NM, et al; for the American College of Rheumatology. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum*. 2008;59:762–784.

Disclosure

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